9 Food Contamination

9.1 General Remarks

Special attention must be paid to the possibility of contamination of food with toxic compounds. They may be present incidentally and may be derived in various ways. Examples of such contaminants are:

- Pollutants derived from burning of fossil fuels, radionuclides from fallout, or emissions from industrial processing (toxic trace elements, radionuclides, polycyclic aromatic hydrocarbons, dioxins).
- Components of packaging material and of other frequently used products (monomers, polymer stabilizers, plasticizers, polychlorinated biphenyls, cleansing/washing agents and disinfectants).
- Toxic metabolites of microorganisms (enterotoxins, mycotoxins).
- Residues of plant-protective agents (PPA).
- Residues from livestock and poultry husbandry (veterinary medicinals and feed additives).

Toxic food contaminants might also be formed within the food itself or within the human digestive tract by reactions of some food ingredients and additives (e. g. nitrosamines). Measures required to prevent contamination include:

- Extensive analytical control of food.
- Determination of the sources of contamination.
- Legislation (legal standards to permit, ban, curtail or control the use of potent food contaminants, and the processes associated with them) to establish permissible levels of contaminants.

Toxicological assessment of a contaminant may, for various reasons, be a difficult task. Firstly, sufficient data are not available for all compounds. Also, the possibility of synergistic effects of various substances, often including their degradation products, should not be excluded. Further, the hazard might be influenced by age, sex, state of health and by habitual consumption. Based on these considerations, any nutritional statement about the "tolerable concentration" must take sufficient safety factors into account.

Toxicity assay involves the determination of:

- Acute toxicity, designated as LD_{50} (the dose that will kill 50% of the animals in a test series).
- Subacute toxicity, determined by animal feeding tests lasting four weeks.
- Chronic toxicity, assessed by animal feeding tests lasting 6 months to 2 years.

In chronic toxicity tests attention is especially given to the occurrence of carcinogenic, mutagenic and teratogenic symptoms. The tests are conducted with at least two animal species, one of which is not a rodent.

The upper dosage level for a substance, fed to test animals over their life span and observed for several generations, which does not produce any effect, is designated as the "No Observed Adverse Effect Level" (NOAEL, mg/kg body weight of the animal tested per day or mg/kg feed per day). This level can be used as a basis for estimating the hazard for humans in all cases in which a correlation between dose and effect has been observed. The NOAEL is multiplied by a safety factor (SF: 10^{-1} to 5×10^{-4}, mostly 10^{-2}), with which especially sensitive persons, extreme deviations from the average consumption and other unknown factors are taken into account, giving the toxicologically acceptable dose. It is expressed as the acute RfD (Reference Dose in mg/kg body weight (BW)/day) or as the Acceptable Daily Intake (ADI).

RfD: the acute RfD is the estimated amount of a chemical compound present in food which, related to the body weight and based on all the facts known at the time of the estimation, can be taken in over a short period of time (usually during a meal or a day) without posing a discernible risk to the consumer's health.

ADI: the ADI value denotes the amount of substance which the consumer can take in every day and lifelong with food without discernible injury to his health.
Taking the consumption habits into account, the RfD can be used to calculate the tolerable concentrations (TC) of substances for individual foods:

$$TC = \frac{NOAEL \times FV}{SF} \times \frac{BW}{CA \times ASF}$$

In this formula, TC is the toxicological tolerable concentration for a particular food (expressed in mg/kg food); NOAEL, no observed adverse effect level (mg/kg feed); FV, daily intake of feed by test animals (kg feed/kg body weight); SF, safety factor (10–2000, but usually 100); BW, body weight of an adult (50–80 kg); CA, amount in kg consumed per day of the food for which the TC is being calculated; and ASF, additional safety factor (up to 10) for particularly sensitive persons, such as children or the sick. The maximum concentrations of contaminants (MRL, maximum residue limit in mg/kg food) allowed by legislation are often still well below toxicological tolerance concentrations because other parameters such as "good agricultural practice" are taken into account.
The ADI value is compared with the NEDI or IEDI value (national or international estimated daily intake) to check the risk which comes from contaminants, e. g., pesticides. If the last mentioned value is higher than the ADI, tests are conducted to find out if there is in fact a risk, which would then lead to further measures, if necessary. In many countries, food monitoring is carried out for the early detection of possible danger due to undesirable substances like plant-protective agents (PPA), heavy metals and other contaminants. Foods belonging to the most important groups of goods are repeatedly tested for the presence of certain contaminants. The results are published on the internet; cf. www.bvl.bund.de.

9.2 Toxic Trace Elements

9.2.1 Arsenic

From the viewpoint of its frequency in the environment, toxic activity and the probability of man's exposure to the substance, arsenic was first on the list of dangerous substances compiled in the USA in 1999. Arsenic was followed by lead, mercury, vinyl chloride, benzene, PCBs, cadmium and benzo[α]pyrene (source: Agency for Toxic Substances and Disease Registry, ATSDR). The amount of arsenic which is probably not dangerous when taken orally is estimated at 0.3 µg/kg body weight/day.

9.2.2 Mercury

Mercury poisoning caused by food intake is derived from organomercury compounds, e. g., dimethyl mercury (CH_3—Hg—CH_3), methyl mercury salts (CH_3—Hg; X = chloride or phosphate), and phenyl mercury salts (C_6H_5—Hg—X; X = chloride or acetate). These highly toxic compounds are lipid soluble, readily absorbed and accumulate in erythrocytes and the central nervous system. Some are used as fungicides and for treating seeds (seed dressing). Methyl mercury compounds are also synthesized by microflora from inorganic mercury salt sediments found on lake and river bottoms. Hence, the content of these compounds might rise in fish and other organisms living in water.
The natural mercury level in the environment appears to have stabilized in the last 50 years. Poisonings recorded in Japan appear to have been caused by consumption of fish caught in waters heavily contaminated by mercury-containing industrial waste water, and in Iraq by milling and consuming seed cereals dressed with mercury, which were intended for sowing. The tolerable dose for an adult of 70 kg is 0.35 mg Hg per week, of which a maximum of 0.2 mg may be derived from the highly toxic methyl mercury. The average mercury intake with food, most of which consumed fish, is shown in Table 9.1

9.2.3 Lead

The contamination of the environment with lead is increased by industrialization and by emissions from cars running on leaded gasoline. Tetraethyllead [$(C_2H_5)_4Pb$], an antiknocking additive used to increase the octane value of gasoline,

is converted by combustion into PbO, $PbCl_2$ and other inorganic lead compounds. The major part of these compounds is found in an approx. 30 m wide band along roads or highways; the lead level sharply decreases beyond this distance. At a distance of 100 m from a road with heavy traffic, the lead level in the atmosphere decreases by a factor of 10 and that in soil and plants by a factor of 20 from the level found at or close to the road. A decrease in the level of lead in gasoline and increased use of unleaded gasoline has resulted in a drop in the extent of contamination. Environmental lead contamination has not, however, significantly increased the level of lead in food. The lead in soil is rather immobilized; thus the increase in the lead level of plants is not proportional to the extent of soil contamination. Vegetables with larger surface areas (spinach, cabbage) may contain higher levels of lead when cultivated near the lead emission source. When contaminated plants are fed to animals, the body does not absorb much lead since most is excreted in feces.

Further sources of contamination are leadcontaining tin cookware and soldered metal cans and lead-containing enamels. This is particularly so in contact with sour food. These sources of contamination are of lesser importance.

1.75 mg of lead are considered as the tolerable weekly dose for adults of 70 kg. The lead content of food is shown in Table 9.1.

Hair and bone analyses have revealed that lead contamination of humans in preindustrialized times was apparently higher than today. This might be due to the use in those days of lead pipes for drinking water, lead-containing tinware, and excessive use of lead salts for heavily glazed pottery used as kitchenware.

Table 9.1. Intake of lead, mercury and cadmium through food consumption[a]

Country	Year[b]	µg/Person × Week
	Lead	
Germany	1988–92	85–544
Finland	1975–78	460
	about 1990	85
Great Britain	1994	170
The Netherlands	1988–89	168–175
Sweden	1987	119
USA	1990–91	29
	Mercury	
Germany	1986	117
	1988	<70
	1988	
	1988	8, 61[c]
Great Britain	1994	28
The Netherlands	1984–86	5
Sweden	1987	13
USA	1986–1991	19,5
	Cadmium	
Germany	1986	192
	1988–91	49–99
Great Britain	1994	96
Japan	1992	189–245
The Netherlands	1988–89	84–112
Sweden	1987	84
USA	1986–91	90

[a] Source: J.F. Diehl (cf. Literature, Chap. 9).
[b] Year of the investigation.
[c] Daily consumption of fish.

9.2.4 Cadmium

Cadmium ions, unlike Pb^{2+} and Hg^{2+}, are readily absorbed by plants and distributed uniformly in all their tissues, thus decontamination by dehulling or by removal of outer leaves, as with lead, is not possible. Certain wild mushrooms (horse mushrooms, giant mushrooms etc.), peanuts and linseed can contain larger amounts of cadmium. The finer the linseed is ground, the higher the intake of cadmium on consumption. The contamination sources are industrial waste water and the sludge from plant clarifiers, which is often used as fertilizer. The cadmium content of food is compiled in Table 9.1.

A prolonged intake of cadmium results in its accumulation in the human organism, primarily in liver and kidney. A level of 0.2–0.3 mg Cd/g kidney cortex causes damage of the tubuli. The tolerable weekly dose for an adult (70 kg) is considered to be 0.49 mg of cadmium. On the whole, the concentrations of the toxic trace elements lead, mercury and cadmium in food show a clearly decreasing tendency, especially in recent studies. This is partly due to improvements

in trace analyses, but also due to a real decrease in food.

9.2.5 Radionuclides

It is estimated that the average radiation exposure in FR Germany in 1975 was 172 mrad, of which 21 mrad were ascribed to internal radiation by natural radionuclides incorporated in the body (about 90% from ^{40}K, the rest from ^{14}C) and less than 1 mrad by nuclides acquired as a result of atmospheric fallout from nuclear explosion tests (50% from ^{137}Cs, a radionuclide with a half life of 30 years, but quickly excreted by the body; approx. 50% from ^{90}Sr, a most dangerous radioisotope, capable of inducing leukemia and bone cancer; and traces of ^{14}C and tritium). ^{137}Cs and ^{90}Sr are the escort elements of potassium and calcium, respectively. Food contamination with radionuclides in FR Germany had its peak in 1964/65, when the intake in food per day per person was 240 pCi of ^{137}Cs and 30 pCi of ^{90}Sr. Up to the Chernobyl reactor accident in April 1986, the intake was less than 10% of previous values as a result of the moratorium on atmospheric testing of atomic weapons. Radionuclide residues in food were not a health hazard.

For 1986, the accident in Chernobyl caused an additional intake of radionuclides with food that is estimated at (children up to the age of 1 year/adults) 1779/4598 Bq/year of ^{131}J, 986/1758 Bq/year of ^{134}Cs, and 1849/3399 Bq/year of ^{137}Cs. The resulting additional effective equivalent dose for people in the FR Germany is estimated at 0.06–0.22 mSv. In comparison, natural radiation exposure is about 2 mSv per year, of which 0.38 mSv/year is caused by radionuclides in food. As a precaution, maximum activity values of 500 Bq/l and 250 Bq/kg have been stipulated for milk and vegetables respectively. In comparison, the activity of natural radionuclides (mainly ^{40}K) in food is: milk 40–50 Bq/kg, milk powder 400–500 Bq/kg, fruit juice concentrate 600–800 Bq/kg and soluble coffee (powder) >1000 Bq/kg.

The level of tritium infiltrating the biosphere is expected to rise further due to increasing nuclear plant operation worldwide.

9.3 Toxic Compounds of Microbial Origin

9.3.1 Food Poisoning by Bacterial Toxins

Most (60–90%) cases of food poisoning are bacterial in nature. They are distinguished by food intake causing:

- Intoxication (poisoning, e. g., by *Clostridium botulinum, Staphylococcus aureus*).
- Diseases caused by massive pollution with facultative pathogenic spores, e. g., *Clostridium perfringens, Bacillus cereus.*
- Infections by *Salmonella* spp. or *Shigella* spp., *Escherichia coli.*
- Diseases of unclear etiology, such as those from *Proteus* spp., *Pseudomonas* spp.

The harmful activity of these bacteria in the digestive tract is ascribed to enterotoxins, which are classified into two groups: exotoxins (toxins excreted by microorganisms into the surrounding medium) and endotoxins (retained by the microorganism cells but released when the cell disintegrates).

Exotoxins are released primarily by grampositive bacteria during their growth. They consist mostly of proteins which are antigenic and very poisonous. They become active after a latent period. This group includes the toxins released by *Clostridium botulinum* (botulin toxin, a globular protein neurotoxin), *Cl. perfringens* and *Staphylococcus aureus.* Table 9.2 gives some important data for these microorganisms, including harmful effects. Intoxications with *St. aureus* are the most frequent cause of food poisoning. Symptoms are vomiting, diarrhea and stomach ache and are caused primarily by food of animal origin (meat and meat products, poultry, cheese, potato salad, pastry).

Endotoxins are produced primarily by gramnegative bacteria. They act as antigens, are firmly bound to the bacterial cell wall and are complex in nature. They have protein, poly-saccharide and lipid components. Endotoxins are relatively heat stable and are in general active without a latent period. The toxins causing typhoid and paratyphoid fevers, salmonellosis and bacterial dysentery are in this group. Salmonellosis is very serious. It is an infection by toxins of about 300 different but closely related organisms. The infec-

Table 9.2. Food poisoning by bacterial toxins

Microorganism:	*Staphylococcus aureus*	*Clostridium botulinum*	*Bacillus cereus perfringens*	*Clostridium*	*E. coli 0157:H7*
Growth conditions					
temperature range	10–45 °C	4–35 °C	10–45 °C	12–52 °C	8–45 °C
pH range	4.5	5		5–8.5	4.0–7.5
Toxin					
type	Protein	Protein	Lipid (?)	Protein	Protein
effective amount	0.5–1 µg	0.1–1 µg	10^8 spores/g	10^6 spores/g	
stability	Relatively thermostable	Thermolabile, inactivation at 80 °C/30 min or 100 °C/5 min			
Incubation time	2–6 h	1–3 days	1–12 h	8–24 h	1 day
Duration of disease	1–3 days	Death after 1–8 days, with survivors ill 6–8 months	0.5–1 day	0.5–1 day	1–3 days first symptoms 2 days – ? disease
Symptoms	Vomiting, diarrhea, abdominal pain	Paralysis of the nerve centres of the *medulla oblongata*	Abdominal pain, nausea, diarrhea, vomiting	Diarrhoe, abdominal convulsions, nausea, loss of appetite	Severe diarrhoe, destruction of erythrocytes
Foods usually accounting for poisoning	Cold meat and cheese slices, mildly acidic salads (meat, poultry, sausage, cheese, potatoes), mayonnaise, cream fillings in baked products	Homemade canned meat, hind bony ham, sliced sausages, trout fillets, canned green beans	Institutional/ community catering: Heated and warmed dishes, cereal containing dishes (corn, rice)	Institutional/ communal catering: Heated and warmed meat dishes, warm desserts, puddings, cream fillings in baked products	Insufficiently heated meat, raw milk, unpasteurized apple juice, unwashed fruit and vegetables

tion is characterized by enteric fever, gastroenteritis and salmonella septicemia. Sources of infections are egg products, frozen poultry, ground or minced beef, confectionery products and cocoa.

Although the bacterium *E. coli* first served only as an indicator of fecal contamination, it has meanwhile received special attention. This bacterium also includes enterotoxic strains, e. g., the especially dangerous strain 0157:H7 discovered in 1983 (Table 9.2).

9.3.2 Mycotoxins

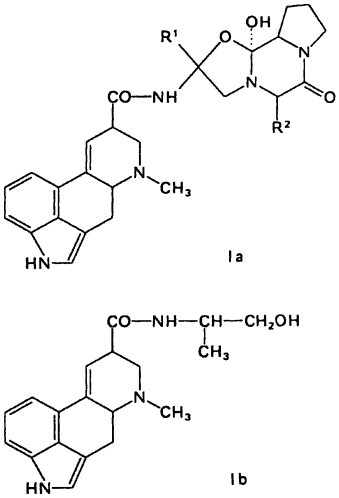
There are more than 200 mycotoxins produced under certain conditions by about 120 fungi or molds. Table 9.3 presents data on mycotoxins of particular interest to food preservation and storage. The chemical structures of these toxins are presented in Fig. 9.1.

Infections of rye and, to a lesser extent, of other cereal grains with *Claviceps purpurea* (ergot, or rooster's spur) are responsible for the disease called ergotism (symptoms: gangrene and convulsions). The disease was important in the past when bread from infected rye grain was eaten. It has practically ceased to exist due to seed treatment with fungistatic agents and grain cleaning prior to milling.

Most mycotoxin data are on the genera *Aspergillus spp.* and the aflatoxins they produce during growth. These are the most common and highly toxic fungal toxins, e. g., aflatoxin B_1, the most powerful carcinogen known. In animal feeding tests with rats, its carcinogenic effect is revealed at a daily dose of only 10 µg/kg body weight. In a comparative study, the carcinogenic property of the highly toxic dimethylnitrosamine was revealed only at a daily dose of 750 µg/kg body weight. It is primarily plant material (particularly nuts and fruit) that is contaminated with aflatoxins. Aflatoxin passes from moldy feed to animal products, primarily milk. The dairy cow's metabolism converts the B-group aflatoxins to those of the M-group ("M" stands for metabolite), which are also carcinogenic. Nephrotoxic ochratoxin A passes from fodder cereals mainly to the blood and kidney tissue of pigs, but it is also found in the muscles, liver and adipose tissue.

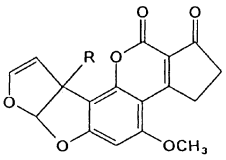
In the course of food monitoring between 1995 and 2002, more than 40 foods were tested for the presence of aflatoxins, deoxynivalenol, fumosins, patulin, ochratoxin A und zearalenone. Individual mycotoxins were detected in 21% of the samples; pistachios were especially conspicuous.

An assessment of the health hazards caused by mycotoxins is not meaningful when applied to the aflatoxins because these substances damage DNA, are carcinogenic and have no threshold below which no harmful effects are observed. An assessment was possible in the case of deoxynivalenol und ochratoxin A, with the reservation

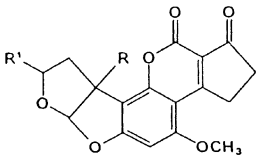


I: Alkaloids of Ergot
Ia: Ergocristine ($R^1 = CH(CH_3)_2$, $R^2 = H_2C-C_6H_5$), Ergostine ($R^1 = C_2H_5$, $R^2 = H_2C-C_6H_5$), Ergotamine ($R^1 = CH_3$, $R^2 = H_2C-C_6H_5$), Ergocryptine ($R^1 = CH(CH_3)_2$, $R^2 = H_2C-CH(CH_3)_2$), Ergocornine ($R^1 = CH(CH_3)_2$ $R^2 = CH(CH_3)_2$), Ergosine ($R^1 = CH_3$, $R^2 = CH_2-CH(CH_3)_2$) Ib: Ergometrine

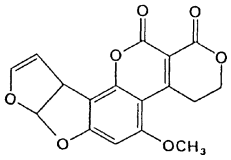
Fig. 9.1. Structures of some mycotoxins (cf. Table 9.3)



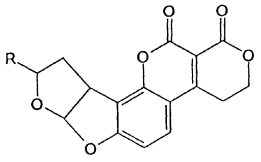
IIa



IIb

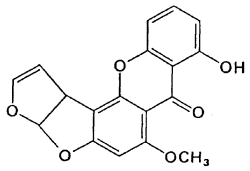


IIc

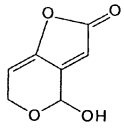


IId

II: Aflatoxins
IIa: Aflatoxin B_1 (R=H), Aflatoxin M_1 (R=OH), IIb: Aflatoxin B_2 (R, R¹=H), Aflatoxin M_2 (R=OH, R¹=H), Aflatoxin B_{2a} (R=H, R¹=OH), IIc: Aflatoxin G_1, IId: Aflatoxin G_2 (R=H), Aflatoxin G_{2a} (R=OH)

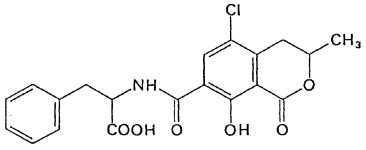


III



IV

III: Sterigmatocystine
IV: Patuline



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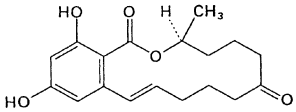
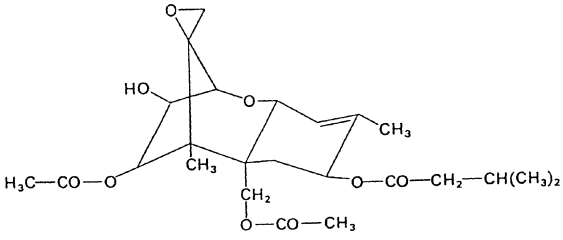
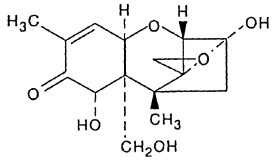


VI

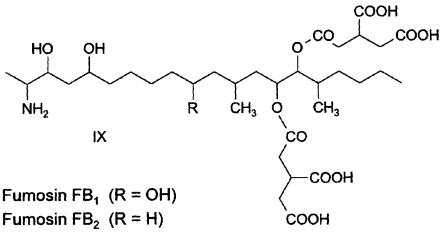


VII



VIII

V: Ochratoxin A
VI: trans-Zearalenone
VII: Fusariotoxin T_2
VIII: Vomitoxin



IX

IX: Fumosin FB_1 (R = OH)
Fumosin FB_2 (R = H)

Fig. 9.1. (Continued)

Table 9.3. Mycotoxins

Fungus/mold	Toxin[a]	Toxicity[b]	Effect	Occurrence
Claviceps purpurea	Ergot alkaloids (I)		Ergotism (gangrenous convulsions)	Mainly rye, to a lesser extent wheat
Aspergillus flavus *A. parasiticus*	Aflatoxins (II)	7.2 mg/kg (rat, orally)	Liver cirrhosis, liver cancer	Groundnuts and other nuts (almond, Brasil nut) corn and other cereals, animal feed, milk
Aspergillus versicolor *A. nidulans*	Sterigmatocystin (III)	120 mg/kg (rat, orally)	Liver cancer	Corn, wheat, animal feed
Penicillium expansum *P. urticae*	Patulin (IV)	35 mg/kg (mouse, orally)	Cellular poison	Putrifying fruits, fruit juices
Byssochlamis nivea, *B. fulva*				
Aspergillus ochraceus *A. melleus*	Ochratoxin A (V)	20 mg/kg (rat, orally)	Fatty liver and kidney damage	Barley, corn
Fusarium graminearum	Zearalenone (VI) (Fusariotoxin F_2)	0.1 mg/kg over 5 days (swine, orally[c])	Estrogen, infertility	Corn and other cereals, animal feed
Fusarium oxysporum *F. tricinctum*	Fusariotoxin T_2 (VII)	3.8 mg/kg (rat, orally)	Toxic aleukia, hemorrhagic syndrome	Cereals, animal feed
Fusarium roseum *F. graminearum*	Deoxynivalenol (VIII) (Vomitoxin)	70 mg/kg (mouse)	Vomiting	Cereals, animal feed
Fusarium moniliforme	Fumosin FB_1 and FB_2 (IX)		Liver cancer	Corn

[a] Roman numerals refer to the structural formulas in Fig. 9.1.
[b] Acute toxicity (LD_{50}).
[c] Estrogenic activity.

Table 9.4. Reference values and their utilization for two mycotoxins (food monitoring 1995–2002)

Substance	Reference[a]	Reference value (μg/kg kg/d)	Utilization (%)
Deoxynivalenol	PMTDI	1	34.1–82.5
Ochratoxin A	PTDI	0.005	7.4–16.1

[a] P(M)TDI: provisional (maximum) tolerable daily intake

that (provisional) defined reference values were assumed. The reservation referred to the fact that the data base for a sound evaluation of the effects on human health is still too limited.

The food intake must be known in order to calculate the utilization of the reference values. For this purpose, a large national study on consumption was carried out in the FRG between 1985 and 1988. With regard to the preferred foods, the amount consumed and the average body weight of the test persons were evaluated. For a differentiated presentation of the results, the test persons were divided into a total of 10 different age, sex and consumption groups, e.g., children, men, women. Among the men and women, a distinction was also made between the meat, fish and fruit eaters (cf. 9.4.4.2).

Table 9.4 shows that in the case of deoxynivalenol, the utilization of the reference value is relatively high at 34.1–82.5%. The upper value was calculated for 4–6 year old children and the lower value for women (fish eaters). Cereal products are mainly contaminated with deoxynivalenol. Ochratoxin A is also most frequently taken in by children. In addition to cereal products, especially fruit juices play a role as a source of this substance.

In comparison with the usual HPLC/UV method, it has been shown in the analysis of mycotoxins using patulin (IV in Fig. 9.1) that the detection limit decreases by a factor of 100 if an isotopic dilution assay (cf. 5.2.6) is carried out with [$^{13}C_2$] patulin as the internal standard. After silylation and gas chromatographic/mass spectrometric measurement of analyte and isotopomer, 5.7–26.0 μg/l of patulin were found in apple juices.

9.4 Plant-Protective Agents (PPA)

9.4.1 General Remarks

The term PPA includes all the compounds used in agricultural food production to protect cultivated plants from plant- and insect-caused diseases, parasites or weeds, or from detrimental microorganisms. The most important groups of PPA are: (1) *herbicides* to protect the plant from weeds; (2) *fungicides* to suppress the growth of undesired fungi or molds; and (3) *insecticides* to protect the plants from damage caused by insects. In addition to these main groups, there are *acaricides* to control mites, *nematocides* to control worms or nematodes, *molluscicides* to protect the plant from snails and slugs, *rodenticides* to control rodents (mice or rats), and plant *growth regulators* (cf. 18.1.4). In Germany in 2003, the herbicides had the largest market share at 43%, followed by the fungicides (28%), insecticides (18%) and the growth regulators (9%). The remaining agents accounted for 2%.

The use of PPA is rewarding since it reduces losses in crop yield and stocks. It has also contributed to the control or eradication of insect-spread diseases such as malaria. Without pest control, the harvest losses of rice, which is especially susceptible, would be 24%. The use of PPA reduces rice losses to 14% and wheat, soybean and corn losses to 7–10%. Apart from losses during cultivation, about 15% of the world harvest is lost during storage due to pests in barns and silos. The substances applied must be effective against pests but safe for the user, consumer and the environment. Accordingly, these substances are evaluated with regard to their toxicological and ecological properties in the registration procedure. Their influence on, e. g., beneficial organisms, aquatic organisms, birds and mammals is tested and their degradability in the soil or in the plant is determined. Since the registration of pesticides has to be renewed at certain times and the costs of the re-evaluation have to be carried mainly by the manufacturer, only those substances which are successful on the market are put through this procedure.

PPA are applied in various forms and by various means: dusting as powder, fumigation, spraying as a liquid, or pad or furrow irrigation. The strict observance of directions for use, waiting

the recommended time between final application and harvest, and restricting the application to the necessary dose, is required to maintain the residual pesticide levels in food at a minimum. Legal regulations with bans on use, stipulated maximum permissible quantities (MRL) etc. emphasize these requirements.

Contamination of food of plant origin can occur directly by treating the crop before storage and distribution (fruit and vegetable treatment with fungicides, cereal treatment with insecticides). It can occur indirectly by uptake from the soil of residual PPA by the subsequent crop, from the atmosphere or drifting from neighboring fields, or from a storage space pretreated with PPA.

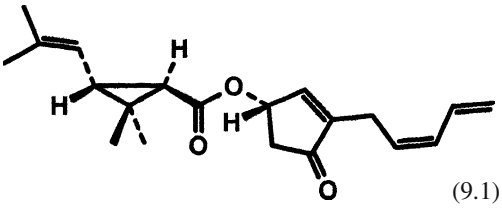
Contamination of food of animal origin occurs by ingestion of feed containing stall- and barn-cleansing agents (fungicides, insecticides), by coming in contact with wooden studs and boards preserved with fungistatic agents, and veterinary medicines and, occasionally, by use of disinfected corn as fodder.

The structures of the PPA mentioned in the following sections are shown in Table 9.5 and Fig. 9.2. Comprehensive details on PPA are given on the internet at www.hclrss.demon.co.uk/index.html and http://extoxnet.orst.edu/pips/ghindex.html and by Tomlin (cf. Literature), who has listed more than 800 compounds.

9.4.2 Active Agents

9.4.2.1 Insecticides

Organophosphate compounds (e.g., IX, XXX, XXXVII, XXXIX in Table 9.5), carbamates (e.g., VII) and pyrethroids (e.g., XIII) have been used as insecticides for many years. The pyrethroids are synthetic modifications of pyrethrin I (cf. Formula 9.1), the main active agent of pyrethrum. Pyrethrum is isolated from the capitulum of different varieties of chrysanthemums and used as a natural insecticide.



(9.1)

Chlorinated hydrocarbons like dichlorodiphenyltrichloroethane (DDT, XII) und lindane (XXVIII) belong to those pesticides which are no longer approved in the EU and the USA. Exceptions are made worldwide only for the use against mosquitoes to control malaria and only if no alternatives are available. The reason for the rejection of chlorinated hydrocarbons is their persistence. They are stable and accumulate in human beings and animals (in the fat phase) and in the environment. The half life DT_{50} (time for 50% dissipation of the initial concentration) of DDT is 4–30 years. In comparison, the DT_{50} values of the organophosphates, carbamates and pyrethroids are in the range of days to a few months, e.g., chlorpyriphos (IXa, b) 10–120 days, carbofuran (VII) 30–60 days and deltamethrin (XIII) <23 days. In Germany, the ban on DDT has resulted in a decrease in the concentration of DDT and its degradation product DDE (cf. 9.4.3) in human milk (mg/kg milk fat) from 1.83 (1979–81) to 0.132 (2002).

Pest populations which are resistant to the active agents develop on longer application. Therefore, new active agents have to be continually synthesized to calculate this resistance. Examples are indoxacarb (XXV) and tebufenozide (XLIII).

Insecticides are mainly nerve poisons. In particular, the older active agents, e.g., parathion (XXXVII, introduced in 1946), chlorpyriphos (IXa, 1965) and methidation (XXXIV, 1965) are also very toxic to mammals (compare acute toxicity LD_{50} in Table 9.5). The toxicity falls when the ethyl groups in IXa are replaced by methyl groups (compare LD_{50} of IXa and b in Table 9.5). Nerve poisons inhibit acetylcholine esterase, bind to receptors which are controlled by the neurotransmitter acetylcholine or interfere with the neurotransmission in the nervous system by modifying the ion canals (examples in Table 9.5). Other insecticides damage the respiratory chain. As mitochondrial uncouplers, they prevent the formation of a proton gradient (Table 9.5). Another mechanism of action is directed at the development of the pests, which can be prevented, e.g., by inhibiting the biosynthesis of chitin.

9.4.2.2 Fungicides

Real fungi (Ascomycetes, Basidomycetes, Deuteromycetes) and lower fungi (Oomycetes)

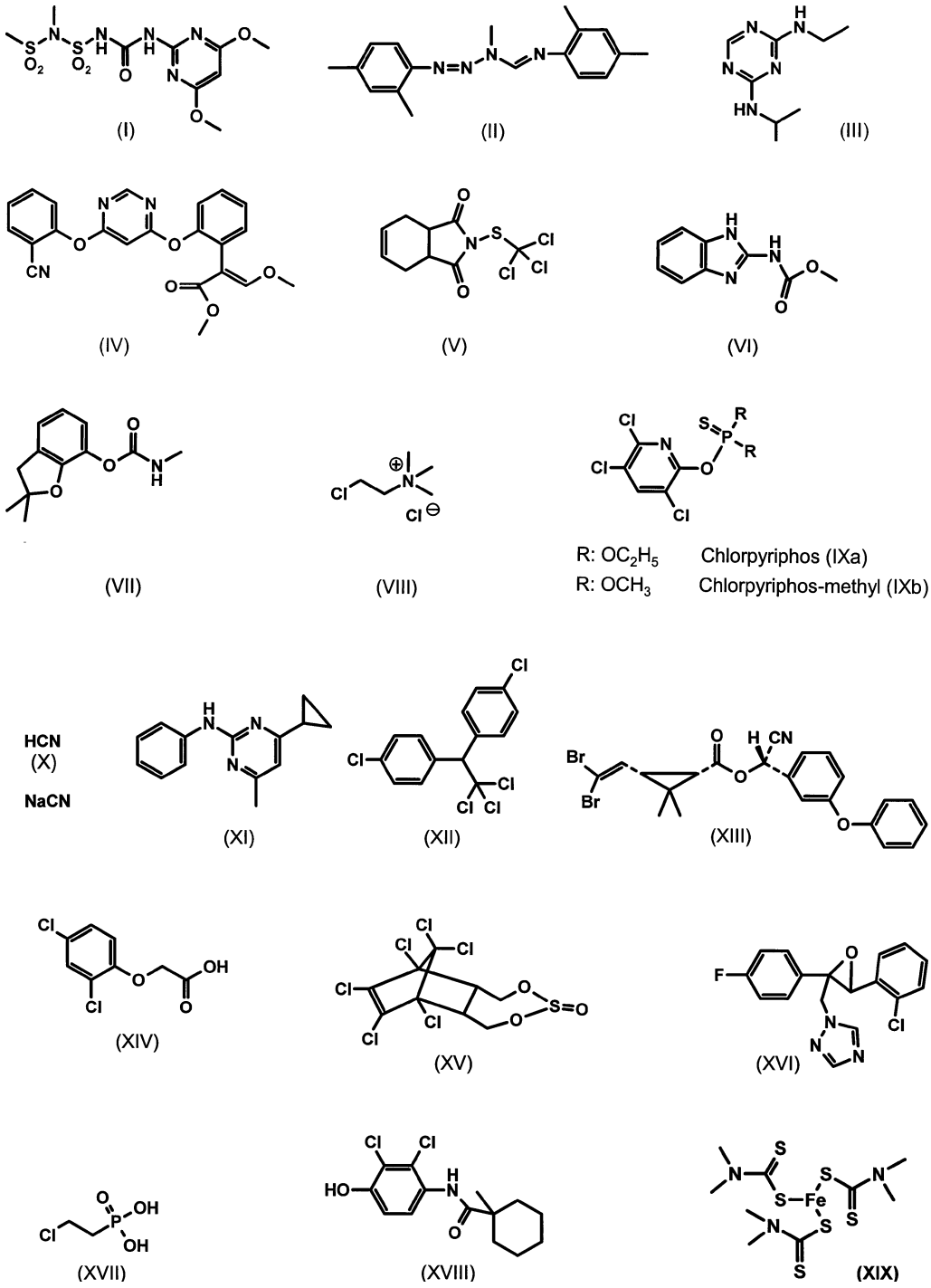
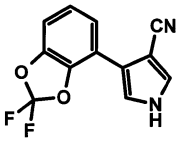
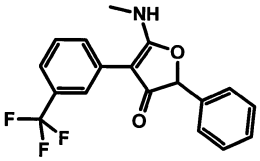


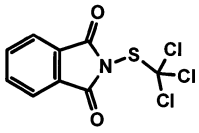
Fig. 9.2. Structures of some selected PPA. The Roman numerals refer to Table 9.5 – sheet 1



(XX)



(XXI)



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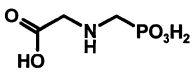

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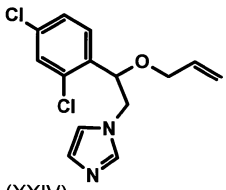

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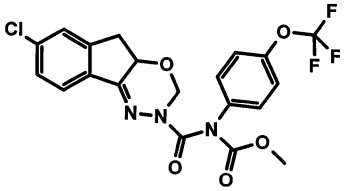

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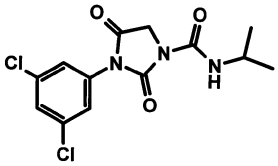

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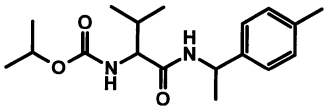

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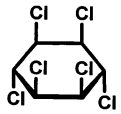

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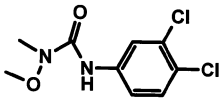

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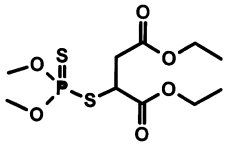

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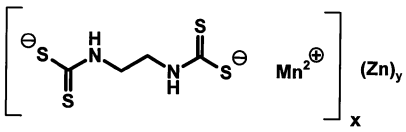

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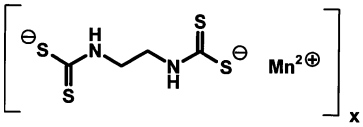

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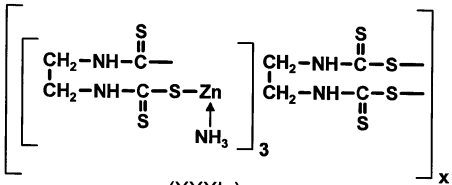

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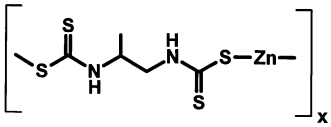
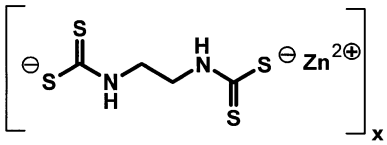
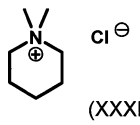


(XXXId)



(XXXIe)

Fig. 9.2. (Continued)



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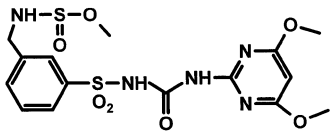

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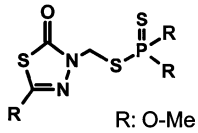

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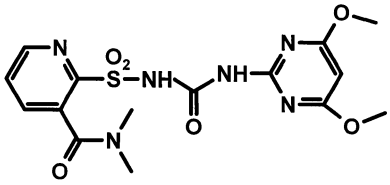
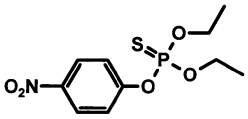


CH_3-Br

(XXXV)

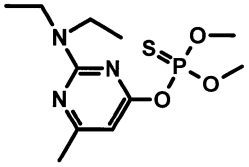
(XXXVI)



(XXXVII)

PH_3

(XXXVIII)



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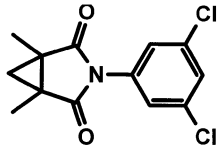

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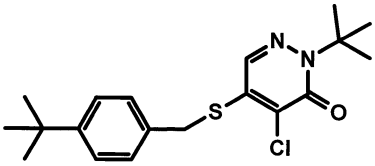

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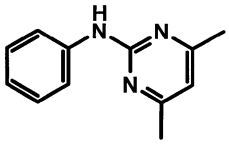

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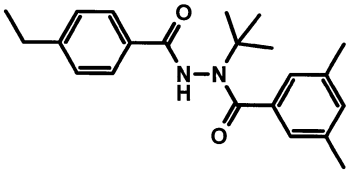

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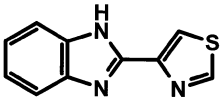

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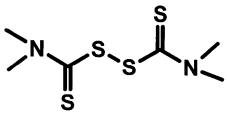

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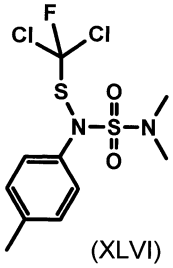

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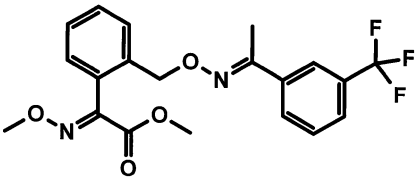

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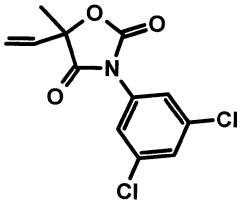

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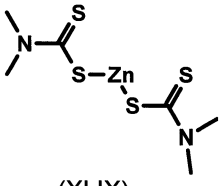


(XLIX)

Fig. 9.2. (Continued)

Table 9.5. Selected PPA

No.	Name	Application[a]	Biochemical activity	LD_{50} (mg/kg)[b]
I	Amidosulfuron	H	Inhibits synthesis of branched AA by inhibition of acetolactate synthase	≥5000 (R, M)
II	Amitraz	I, A	Nerve poison	650 (R)
III	Atrazine	H	Inhibits electron transport in photosystem II	1869–3090 (R)
IV	Azoxystrobin	F	Inhibits the respiratory chain	>5000 (R, M)
V	Captan	F	Inhibits respiration	9000 (R)
VI	Carbenedazine	F	Inhibits β-tubulin biosynthesis	6400 (R), >2500 (H)
VII	Carbofuran	I, N	Choline esterase inhibitor	8 (R), 15 (H)
VIII	Chloromequat	Pgr	Inhibits gibberellin biosynthesis	807–966 (R)
IXa	Chlorpyriphos	I	Choline esterase inhibitor	135–163 (R), 1000–2000 (K)
IXb	Chlorpyriphos methyl	I, A	Choline esterase inhibitor	>3000 (R), 1100–2250 (M)
X	Cyanide	I, R	Prevents O_2 transport by hemoglobin into the cell	6–15 (R)
XI	Cyprodinil	F	Probably inhibitor of methionine synthesis	>2000 (R)
XII	DDT	See text	Nerve poison	113–118 (R), 500–570 (H)
XIII	Deltamethrin	I	Nerve poison: inhibits the function of Na^+ ion channels	>2000 (R), >300 (H)
XIV	2,4-Dichlorophenoxyacetic acid (2,4-D)	H	Inhibits growth	639–764 (R)
XV	Endosulfan	I, A	Antagonist for the GABA receptor[c]	70–240 (R)
XVI	Epoxiconazole	F	Inhibits sterol biosynthesis	>5000 (R)
XVII	Ethephon	Pgr	Decomposes to ethylene	3030 (R)
XVIII	Fenhexamide	F	Inhibits sterol biosynthesis	>5000 (R)
XIX	Ferbam	F		>4000 (R)
XX	Fludioxonil	F	Inhibits MAP kinase[d]	>5000 (R)
XXI	Flurtamone	H	Blocks carotene biosynthesis	500 (R)
XXII	Folpet	F	Inhibits respiration	>9000 (R)
XXIII	Glyphosates	H	Inhibits biosynthesis of aromatic compounds	5600 (R), 3530 (goat)
XXIV	Imazalil	F	Inhibits ergosterol biosynthesis	227–343 (R), >640 (H)
XXV	Indoxacarb	I	Blocks Na channels in nerve cells	1732 (male R), 268 (female R)
XXVI	Iprodion	F	Inhibits germination of spores and growth of mycelium	>2000 (R, M)
XXVII	Iprovalicarb	F	Inhibits growth of Oomycetes fungi	>5000 (R)

Table 9.5. (Continued)

No.	Name	Application[a]	Biochemical activity	LD_{50} (mg/kg)[b]
XXVIII	Lindane (γ-HCH)	See text	Antagonist for the GABA receptor	88–270 (R)
XXIX	Linuron	H	Inhibits electron transport in photosystem II	1500–4000 (R)
XXX	Malathion	I, A	Inhibitor of choline esterase	1375–5500 (R)
XXXI	Maneb group	F	Inactivates SH groups, inhibits respiration	
	a. Mancozeb			>5000 (R)
	b. Maneb			>5000 (R)
	c. Metiram			>5000 (R)
	d. Propineb			>5000 (R)
	e. Zineb			>5200 (R)
XXXII	Mepiquat	Pgr	Inhibits biosynthesis of gibberellic acid	464
XXXIII	Mesosulfuron methyl	H	Inhibits biosynthesis of branched AA like I	>5000
XXXIV	Methidathion	I, A	Inhibits choline esterase	25–54 (R), 25–70 (M)
XXXV	Methylbromide	I, A, R		See legend[e]
XXXVI	Nicosulfuron	H	Inhibits biosynthesis of branched AA like I	>5000 (R)
XXXVII	Parathion	I, A	Inhibits choline esterase	≈2 (R), 12 (M)
XXXVIII	Phosphide/PH3	I, R	Inhibits respiration	8,7 (R)[f]
XXXIX	Pirimiphos methyl	I, A	Inhibits choline esterase	1414 (R), 1180 (M)
XL	Procymidone	F	Inhibits triglyceride biosynthesis in molds	6800 (R)
XLI	Pyridaben	I, A	Inhibits electron transport in the mitochondria	1350 (R)
XLII	Pyrimethanil	F	Inhibits methionine biosynthesis (assumption)	4150–5971 (R)
XLIII	Tebufenozid	I	Antagonist of the insect hormone ecdyson	>5000 (R)
XLIV	Thiabendazol	F	Inhibits mitosis by binding to tubulin	3100 (R)
XLV	Thiram	F		2600 (R), 210 (K)
XLVI	Tolylfluanid	F	Inhibits respiration	>5000 (R)
XLVII	Trifloxystrobin	F	Inhibits the respiratory chain	>5000 (R)
XLVIII	Vinclozolin	F	Prevents germination of spores	>15000 (R, M)
XLIX	Ziram	F	Inactiviates the SH-group	>2000 (R), 100–300 (K)

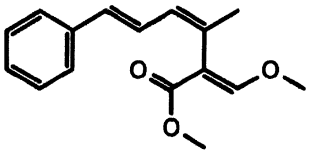
[a] A, acaricide; H, herbicide; I, insecticide; R, rodenticide; Pgr, plant growth regulator.
[b] Mean lethal dose (LD_{50}); experimental animal: H, dog; M, Mouse, R, rat; K, rabbit.
[c] GABA: γ-aminobutyric acid.
[d] MAP kinase: nitrogen-activated protein kinase (participates in mitosis).
[e] Toxic with threshold value for inhalation of 0.019 mg/l air.
[f] LD_{50} for aluminium phosphide.

can destroy entire harvests. These fungi and their spores are controlled by fungicides so that mildew, rust, leaf blight, stem rot, botrytis and other plant diseases do not occur. Depending on the mode of action, a distinction is made between the contact fungicides, which act on the surface of the plant preventing germination and/or penetration of the fungus into the plant, and systemic fungicides, which penetrate into the plant and eliminate hidden seats of disease.

The active agents can be divided into inorganic, organometallic and organic compounds. Inorganic fungicides include Bordeaux mixture, copper chloride oxide, lime sulfur and colloidal sulfur. Examples of organometallic compounds are dithiocarbamates of zinc and manganese (Maneb group; XXXIa–e in Table 9.5), which are relatively often encountered as residues in foods (cf. 9.4.4). Most of the fungicides are, however, metal-free organic compounds (examples in Table 9.5).

In the case of the fungicides, too, the development of resistance necessitates the continual development of new active agents. A special innovation was the introduction of synthetic modifications of the fungal constituent strobilurin A (Formula 9.2), which has antibiotic and fungicidal activity. Examples are azoxystrobin (IV) and epoxyconazole (XVI).

Another new class of substances are the valinamides, which has given rise to the active agent iprovalicarb (XXVII). Information on the toxic activity of these fungicides is given in Table 9.5.



(9.2)

The development of active agents with increased fungicidal activity but constant relatively low toxicity for mammals has led to a considerable reduction of the dose required. The examples in Table 9.6 show that this trend has also been observed for insecticides and herbicides.

PPA residues in foods have most often been found in fruit and vegetables (Table 9.7). Among the identified active agents, the fungicides play the biggest part (Table 9.8). Therefore, special attention has been paid to them in Table 9.5.

Table 9.6. Amounts used of some plant protection agents

Active agent	Introduced in the year	Dose (g/ha)
A. Insecticides		
Chlorpyriphos methyl (IXb)	1966	250–1000
Deltamethrin (XIII)	1984	5–20
Indoxacarb (XXV)	1996	12.5–125
B. Fungicides		
Mancozeb (XXXIa)	1961	1500–3000
Azoxystrobin (IV)	1992	100–375
Epoxyconazole (XVI)	1993	125
C. Herbicides		
2,4-D (XIV)	1942	300–2300
Atrazine (III)	1957	$\leq$1500
Nicosulferon (XXXVI)	1990	35–70

Table 9.7. Foods with pesticide residues which exceeded the permissible upper limit (investigated in 2003 in Germany)[a,b]

Food	N	N_O	N_R	N_H	N_H (%)
A. Cereal					
Barley	23	11	11	1	4.3
Rice	159	126	31	2	1.3
Wheat	301	186	113	2	0.7
B. Food of animal origin					
Poultry meat	583	322	259	2	0.3
Cheese and curd	273	100	172	1	0.4
Mutton	24	11	11	2	8.3
Bird's eggs	324	125	197	2	0.6
C. Fruit and vegetables					
Pineapple	64	23	28	13	20.3
Apple	456	161	277	18	3.9
Apricot	159	54	88	17	10.7
Aubergine	185	122	51	12	6.5
Pear	426	139	243	44	10.3
Cauliflower	123	62	58	3	2.4
Bean with hull	109	62	40	7	6.4
Broccoli	14	12	1	1	7.1
Blackberry	8	0	6	2	25.0
Chinese cabbage	32	18	8	6	18.8
Peas without pods	122	45	66	11	9.0
Strawberry	894	173	663	58	6.5
Fig (dried)	6	3	2	1	16.7
Fennel	10	7	1	2	20.0
Grapefruit	51	22	28	1	2.0
Kale	11	6	2	3	27.3
Cucumber	381	214	140	27	7.1 (11.4)
Hazelnut	39	36	2	1	2.6

Table 9.7. (Continued)

Food	N	N_O	N_R	N_H	N_H (%)
Blueberry	54	41	12	1	1.9
Raspberry	59	27	27	5	8.5
Currant	107	25	67	15	14.0 (17.2)
Cherry	173	101	69	3	1.7
Kiwi	102	47	54	1	1.0
Turnip	64	46	14	4	6.3
Mandarin	233	26	187	20	8.6
Mango	45	25	17	3	6.7
Melon	32	13	18	1	3.1
Orange	209	34	164	11	5.3
Papaya	24	13	4	7	29.2
Bell pepper	922	367	403	152	16.5 (21.5)
Parsley	30	13	12	5	16.7
Peach	271	110	125	36	13.3
Plum	158	93	62	3	1.9
Leek	13	12	0	1	7.7
Rocket	80	8	52	20	25.0 (30.1)
Salad	451	153	255	43	9.5
Asparagus	135	104	29	2	1.5
Spinach	87	72	11	4	4.6
Tomato	691	333	311	47	6.8
Grape	933	157	645	131	14.0 (12.9)
Lemon	300	124	149	27	9.0
Zucchini (courgette)	89	52	34	3	3.4

[a] N: number of samples; N_O: number of samples without detectable residues; N_R: number of samples with residues including the maximum permissible quantity; N_H: number of samples with residues above the maximum quantity; N_H in percent (with reference to: N).
[b] In brackets are the values for 2004.

9.4.2.3 Herbicides

A distinction is made between non-specific and specific herbicides. The former inhibit the growth of both cultivated plants and weeds. For this reason, they can only be used before sowing. The introduction of resistance genes in soybean, corn and rape seed, among others, allows their weeds to be controlled by non-specific herbicides even during growth.

Selective herbicides inhibit the growth of weeds while protecting the cultivated plants. This selective action is achieved, e. g., because, unlike the weed, the cultivated plant quickly degrades the herbicide. One of the first selective herbicides was 2,4-dichlorophenoxyacetic acid (XIV), which eliminates only dicotyledon weeds but not monocotyledon cereal plants.

Newer selectively acting herbicides are the compounds amidosulfuron (I), mesosulfuron methyl (XXXIII) and nicosulfuron (XXXVI), which belong to the class of sulfonyl ureas. Since they are very active, the amount used is very small (compare atrazine (III) and nicosulfuron (XXXVI) in Table 9.6). As in the case of the other PPA, the biochemical mechanism of action of most of the herbicides is known (examples in Table 9.5). They frequently target a reaction site in the chloroplasts.

9.4.3 Analysis

The purpose of the analyses is to detect PPA which are not registered and to expose cases where the stipulated maximum permissible amounts have been exceeded. In addition, it is necessary to continually measure the contamination of food with PPA (monitoring, cf. 9.4.4).

The analysis of PPA residues is difficult because the number of active agents which can be taken into consideration is very large. For example, 255 compounds were registered in Germany in 2003 and maximum permissible amounts were stipulated by law for 600 compounds. However, we have to reckon with the use of about 1000 active agents worldwide. The analysis is made more difficult by the large differences in the chemical structures and the requirement for an exact quantification, the maximum permissible quantities being in the trace range, i. e., between 0.001 and 10 mg/kg. The following example gives an insight into the most important steps of a method (multimethod) with which a series of pesticides are identified.

A sample of a fruit or vegetable (ca. 10 g) is homogenized with the solvent (acetonitrile) which contains the internal standard (triphenyl phosphate). Anhydrous $MgSO_4$ and NaCl are added to bind water. After centrifugation, an SPE (solid phase extraction) sorbent is stirred in an aliquot of the supernatant to bind organic acids, pigments and sugar. After a second centrifugation, the PPA and the internal standard are identified

Table 9.8. Number of food samples with reference to the individual active agent (investigated in 2003 in Germany)[a]

Active agent	N_1	N_2	N_2 (%)	Concentration (mg/kg)
A. Cereal				
Hydrogen cyanide (V)	40	40	100	0.1
Bromide	80	62	77.5	0.25
Chlormequat (VIII)	46	20	43.5	0.01
Ethephon (XVII)	37	12	32.4	0.2
Primiphos methyl (XXXIX)	195	19	9.7	0.02
Flurtamone (XXI)	20	1	5.0	0.005
Phosphide/PH3 (XXXVIII)	28	1	3.6	0.01
DDT (XII)[b]	99	3	3.0	0.2
B. Fruit and vegetables				
Bromide	562	254	45.2	0.01
Chlormequat (VIII)	1416	338	23.9	0.01
Maneb group (XXXI)[c]	1890	367	19.4	0.01
Amitraz (II)	315	49	15.6	0.01
Chlorpyriphos (IXa)	5412	617	11.4	0.01
Carbenedazine (VI)	2608	273	10.5	0.005
Cyprodinil (XI)	3894	396	10.2	0.05
Procymidone (XL)	5264	524	10.0	0.01
Thiabendazole (XLIV)	2621	250	9.5	0.005
Fenhexamide (XVIII)	1460	129	8.8	0.03
Endosulfan (XV)	5363	417	7.8	0.005
Imazalil (XXIV)	4387	314	7.2	0.05
Mepiquat (XXVII)	1127	71	6.3	0.01
Fludioxonil (XX)	3715	216	5.8	0.005
Tolylfluanid (XLVI)	5052	287	5.7	0.001
Captan (V)/Folpet (XXII)	5041	261	5.2	0.01
Pyridaben (XLI)	1692	72	4.3	0.005
Pyrimethanil (XLII)	3399	146	4.3	0.005
Vinclozolin (XLVIII)	5196	199	3.8	0.01
Methidation (XXXIV)	5389	184	3.4	0.02
Trifloxystrobin (XLVII)	1079	36	3.3	0.005

[a] Of the 373 (cereal) or 399 (fruit and vegetables) active agents analyzed, those with $N_2 \geq 3\%$ are listed.
N_1: number of samples; N_2: number of samples with an active agent concentration equal to or higher than the concentration given in the column on the right. N_2 (%): N_2 with reference to N_1.
[b] Including degradation products.
[c] Calculated as CS_2.

and quantified by gas chromatography–mass spectrometry (MS). Alternatively, LC (liquid chromatography)–MS processes are also used to detect the analytes. The LC–MS process is the method of choice in the case of thermolabile active agents. Some pesticides can be accurately identified only by MS–MS measurements.

A series of PPA cannot be identified by a multimethod because their polarity and structural differences are too large. For the analysis of such active agents, special processes have been elaborated, with isotope dilution analyses (principle, cf. 5.2.6.1) also playing a part.

If metabolites of PPA are toxicologically relevant, they are also identified in the analysis, e. g., the degradation product 2,4-dimethylaniline together with the active agent amitraz (II), and dichlorodiphenyldichloroethane (DDD) and dichlorodiphenyldichloroethylene (DDE) with DDT (XII).

On the plant, PPA are exposed to light and can undergo photolysis. An example is parathion (XXXVII). Nitrosoparathion is formed, among other compounds, and reacts with components of the cuticle. The resulting product is insoluble and is not detected by the conventional PPA analysis. It can be identified directly on the cuticle with the help of the ELISA technique (principle, cf. 2.6.3).

9.4.4 PPA Residues, Risk Assessment

9.4.4.1 Exceeding the Maximum Permissible Quantity

In Germany, 12,874 samples were tested for the presence of PPA in 2003. 2515 samples came from the monitoring program (cf. 9.4.4.2) and 10,359 from official food monitoring. No PPA were found in 42.9% of these samples. In 50.1% of the samples, residues were present which were equal to or less than the maximum permissible quantity. Altogether 890 samples (6.9%) had residue content higher than the maximum permissible quantity.

Table 9.7 shows the foodstuffs that were most affected. Thus, the permissible upper limit was exceeded in more than 10% of the samples of pineapples, apricots, pears, blackberries, Chinese cabbage, dried figs, fennel, kale, currants, papaya, bell pepper, parsley, peaches, rocket and grapes. The figures for 2004 are also given for a few foods which were more contaminated.

Table 9.8 shows how often the individual active agents occurred. Hydrogen cyanide, followed by bromide and chloromequat were detected in every sample of cereal. The two last mentioned active agents were found most frequently in fruit and vegetables. The maneb group, amitraz, chlorpyriphos, carbenedazine, cyprodinil and procymidones also accounted for proportions of 10% and more of the samples of these foods. The frequency of bromide is due to the fact that it is a naturally and ubiquitously occurring substance. Higher concentrations can indicate the use of bromine-containing fumigants, e. g., methyl bromide (XXXV), in soil treatment or in storage.

The EU coordinated a pesticide monitoring program with the participation of Norway, Iceland and Liechtenstein in 2002. They investigated the occurrence of a total of 41 pesticides in pears, bananas, oranges/mandarins, peaches/nectarines, beans, potatoes, carrots and spinach.

Residue concentrations higher than the permissible upper limit were found most frequently in spinach (13% of the tested samples), followed by beans (7%), oranges/mandarins (4%) and peaches/nectarines (3%). Of the active agents, residues of the maneb group most often exceeded the permissible upper limit (1.19% of all the tested samples).

In the USA, a monitoring program for insecticides in 2002 showed that DDT (0.0001–0.025 mg/kg) was the most frequently found active agent. It was found in 21% of the samples. Furthermore, chlorpyriphos methyl (17%, 0.0002–0.59 mg/kg), malathion (15%, 0.0007–0.071 mg/kg), endosulfan (14%, 0.0001–0.166 mg/kg) and dieldrin (11%, 0.0001–0.010 mg/kg) occurred in more than 10% of the tested samples.

9.4.4.2 Risk Assessment

The results of the food monitoring program in 1995–2002 were used for the risk assessment. In this time period, 30,682 samples from 130 different foods were analyzed for the presence of 160 PPA. No active substances or only traces were found in 45.7% of the samples. Concentrations exceeding the maximum permissible amounts were determined in 2.6% of the samples.

The PPA selected for the risk assessment were those which were quantified in at least 5% of the samples of three or more foodstuffs. Table 9.9 shows the selection. The calculation of the food intake was based on the results of the national consumption study, which was carried out in the FRG between 1985 and 1988 (cf. 9.3.2).

The overview of the results in Table 9.9 shows that the reference values of the selected PPA are mostly utilized to less than 1%. The dithiocarbamates are the only exception with a utilization of 7.7 to 18.3%. The lower value was found for the group of men (women 9.6%) and the upper value for children (4–6 years of age). The reason for this difference is probably the consumption of fruit because men eat less fruit than children. Fruit can contain residues of dithiocarbamates used for controlling fungal diseases.

Table 9.9. Utilization of the reference value[a] (food monitoring 1995–2002)

Active agent	Reference ADI[b] (μg/kg kg/d)	Utilization (%)
Bromide	1000	0.7–1.3
Carbenedazine (VI)	30	0.2–0.5
Captan (V)/Folpet (XXII)	100	0.03–0.10
Chlorpyrifos (IXa)	10	0.1–0.3
Dithiocarbamates[c]	3[d]	7.7–18.3
Iprodion (XXVI)	60	0.2–0.4
Pirimiphos methyl (XXXIX)	30	0.1–0.3
Procymidon (XL)	100	0.03–0.09
Thiabendazole (XLIV)	100	0.1–0.4
Vinclozolin (XLVIII)	10	0.8–3.5

[a] The utilization (%) is defined as the ratio of the estimated daily intake (μg/d) of an active agent to the appropriate reference value.
[b] ADI: definition cf. 9.1.
[c] Dithiocarbamates: mancozeb (XXXIa), maneb (XXXIb), metiram (XXXIc), zineb (XXXIe), thiram (XLV), ferbam (XIX), ziram (XLIX) and propineb (XXXId).
[d] The ADI value of the dithiocarbamates lies between 3 and 30 μg/kg kg/d. The lowest value was taken as a basis for the calculation.

The German Federal Office for Consumer Protection and Food Safety came to the following conclusion based on the monitoring results: "The utilization of the toxicological reference values (permissible or tolerable daily intake) is without exception very small, being only about 1% for the plant-protective agents and the persistent organochloro compounds tested. A substantial exposure was observed only with the dithiocarbamates. However, it should be taken into account that the results can be partly superimposed by the residues of naturally occurring sulfur-containing substances. The results obtained up to now do not represent the possible total contamination of the consumers with residues of plant protection agents, however a distinct section because the analysis spectrum did not include all the conceivable active substances of plant protection agents and their metabolites, but about 160 substances relevant to foodstuffs."
The latest results of the food monitoring program are to be found in the annually published report on food safety at www.bvl.bund.de

9.4.4.3 Natural Pesticides

The natural pesticides should not be disregarded in the risk assessment. Ames and Gold (2000) have shown that in comparison with the synthetic pesticides, the pesticides occurring naturally in food are of much greater importance. Substances of this type are produced by the plant for protection against microorganisms and insects, e.g., allylisothiocyanate, benzaldehyde, caffeic acid, capsaicin, catechin, estragol, d-limonene and 4-methylcatechin.
These substances include as high a percentage of compounds which are carcinogenic as among the synthetic pesticides. It has been estimated for the USA (the conditions in Europe should be similar) that the population consumes with food on average 1500 mg per person and day of natural pesticides, but only 0.09 mg of synthetic pesticides. In summary, it can be concluded that a risk of impairment of consumer health is not discernible in the case of the proper and controlled application of registered PPA.

9.5 Veterinary Medicines and Feed Additives

9.5.1 Foreword

The current practice in animal husbandry is the wide use of veterinary medicines, which serve not

Table 9.10. Animal medicines (selected structural formulas are presented in Fig. 9.3)

Number	Class of compounds	Example
Antibiotics		
I	Sulfonamides	Sulfapyridine (Ia), Sulfathiazole (Ib)
II	β-Lactams	Amipicillin (IIa), Amoxycillin (IIb)
III	Tetracyclines	Tetraycline (IIIa), Oxytetracycline (IIIb)
IV	Aminoglycosides	Streptomycin (IVa), Dihydrostreptomycin (IVb)
V	Macrolides	Tiamulin (Vt)
VI	Crinolines & Fluorochinolones	Ciprofloxacin (VIa), Marbofloxacin (VIb)
Anthelmintics		
VII	Benzimidazoles	Fenbendazole (VIIa), Mebendazole (VIIb)
VIII	Tetrahydroimidathiazoles	Levamisol (VIIIa), Morantel (VIIIb)
IX	Avermectins	Ivermectin (IX)
Coccidiostats		
X	Different classes	Dicoquinat (Xa), Clopidol (Xb), Lasalocid (Xc)

only for therapy, but to a large extent for prophylaxis and economic aims (e. g. to shorten animal growth or feeding time; to abate the risk of losses). Veterinary preparation residues in food are ingested by humans in low amounts but continuously and, hence, could be a health hazard. This possibility was, for a long time, not carefully examined. Therefore, as in the field of pesticides, supporting and maintaining appropriate measures (imposing legally binding regulations, analytical control or supervision, elucidation of toxicological problems) has the ultimate aim of protecting human health.

A brief outline of some important groups of veterinary medicines follows. Table 9.10 and Fig. 9.3 provide a review of their use and chemical structures.

9.5.2 Antibiotics

Antibiotics are used prophylactically to stem infections, e. g., in intensive mass animal farming and in the therapy of infectious diseases. Since they inhibit the growth of the microflora, which is present in the digestive tract of livestock, feed utilization is improved. The animals gain weight faster. This application of antibiotics as growth promoters is regarded critically in the EU and has led to bans. A constant intake of antibiotics, even at low doses, is a risk to human health since some microorganisms may become resistant and allergic reactions may develop.

9.5.3 Anthelmintics

In meadows and sheds, animals come into contact with their excrements and subsequently with worms in all developmental stages. Anthelmintics are used against the resulting diseases caused by worms.

9.5.4 Coccidiostats

The compounds of this class are added to animal feed to combat coccidiosis diseases (such as enteritis or cachexie) caused by protozoans living as parasites in intestines. Poultry and rabbits are the animals most often affected. Residues may be found in eggs.

9.5.5 Analysis

The aim of these analyses is:

- to detect medicines which are banned or not approved, e. g., chloramphenicol (XIt), nitrofurans (derivatives of 2-nitrofuran, e. g., nitrofurantoin, XIIt), fattening aids with estrogenic activity such as 17-estradiol (XIIIt), diethylstilbestrol (XIVt), zeranol (XVt).
- to check if the residue of an approved therapeutic agent is still within the permissible upper limit (MRL, cf. 9.1).

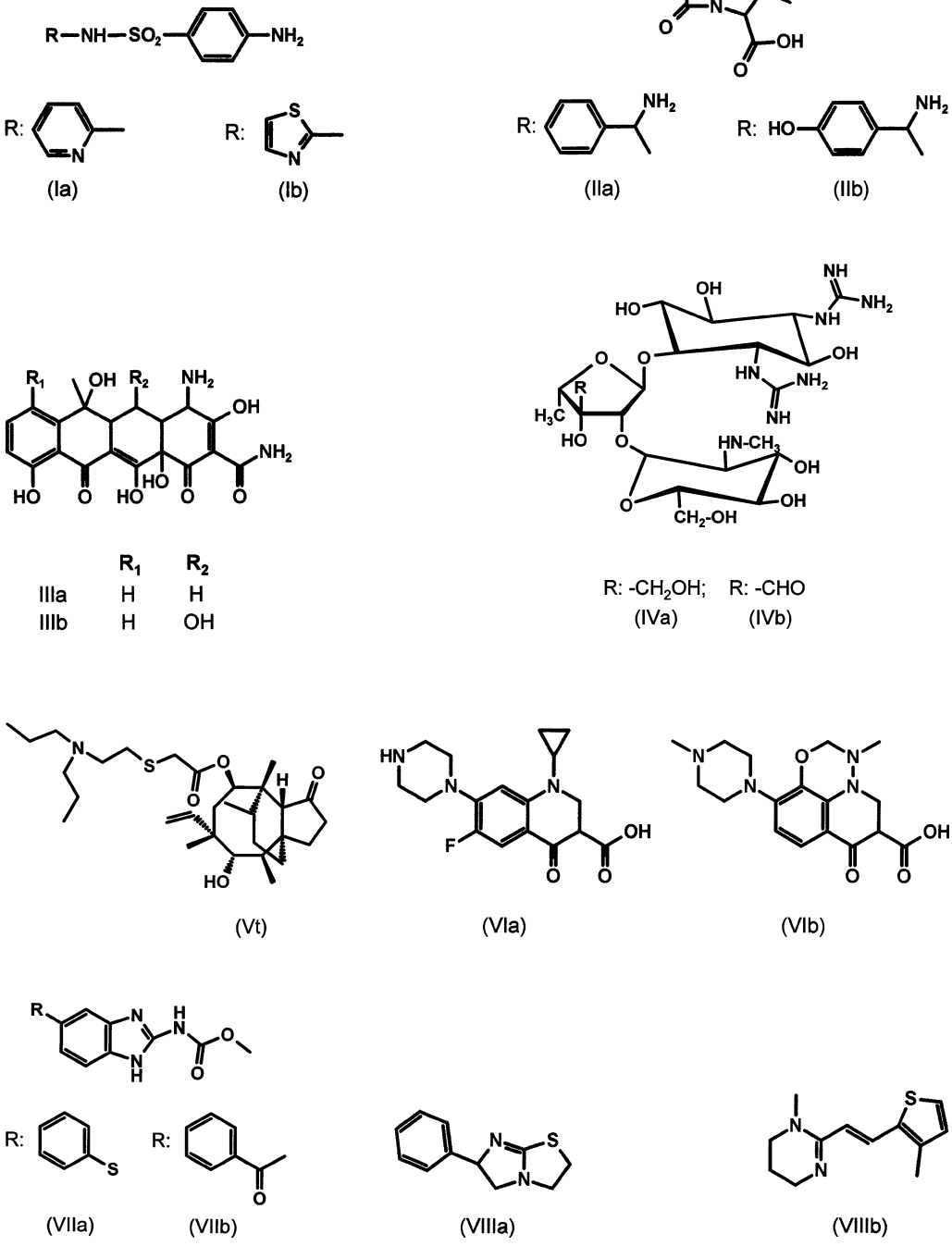


Fig. 9.3. Structures of some selected veterinary medicines. The Roman numerals refer to Table 9.10 and to the text (cf. 9.5.5)

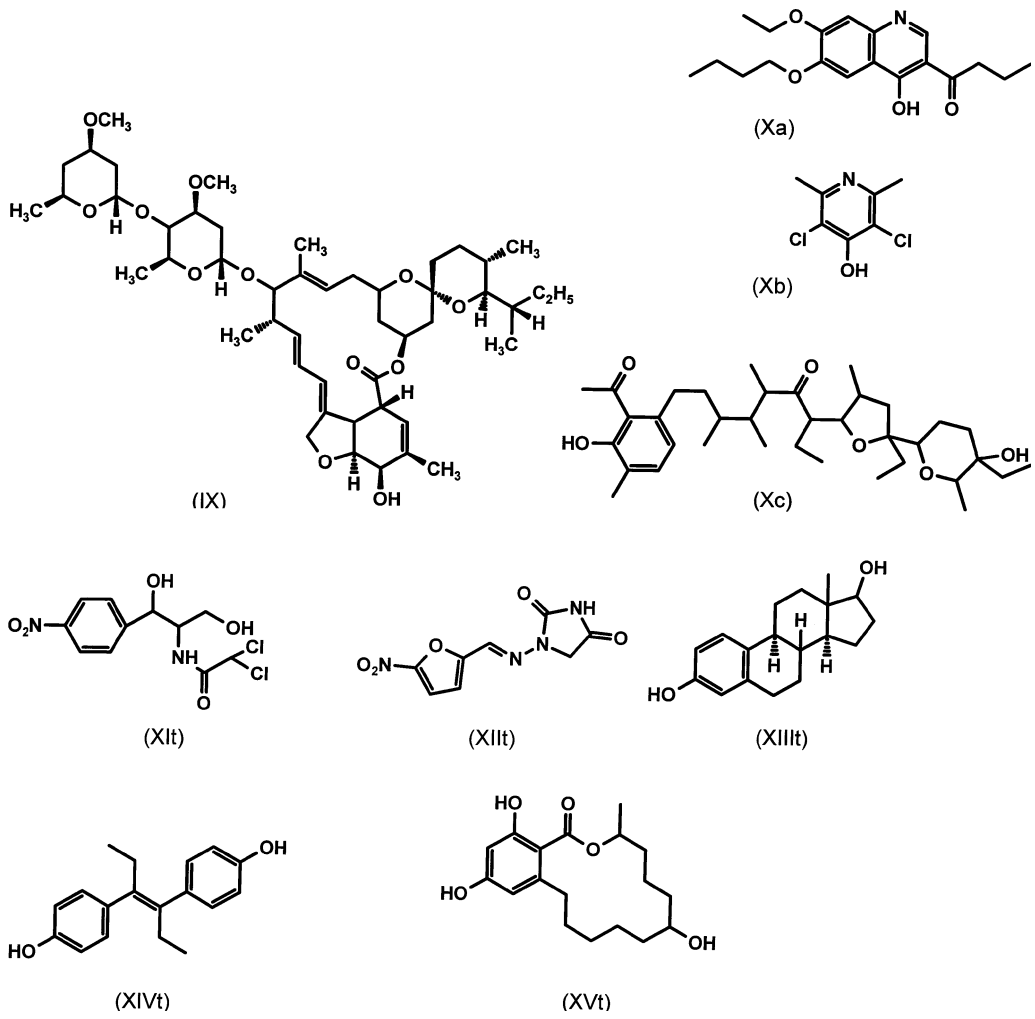


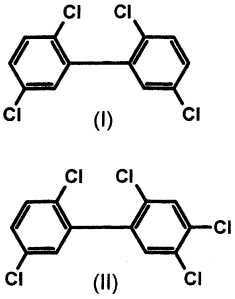
Fig. 9.3. (Continued)

The analysis starts with screening. Antibiotics can be detected with the help of the bacteria whose growth they inhibit. Their differentiation can be further improved by means of an electrophoretic preliminary separation.

In principle, the same isolation and separation methods and mass spectrometric techniques are used for the unambiguous identification of veterinary medicines as for pesticides (cf. 9.4.3). Enzyme immunoassays are also used (cf. 2.6.3).

9.6 Polychlorinated Biphenyls (PCBs)

The PCBs are complex mixtures of substances which have been on the market since 1950. They are widely used, e. g., as transformer oil, hydraulic fluid, heat exchange medium, dielectric fluid in condensers, plasticizer and additive for printing ink. Formula 9.3 shows 2,2′,5,5′-tetrachlorobiphenyl (I) and 2,2′,4,5,5′-pentachlorobiphenyl (II) as examples.



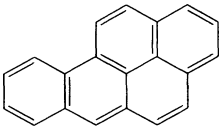
(9.3)

As a result of their widespread use, the PCBs also came into contact with food. Because of their persistence and solubility in fat, they accumulated like in the case of DDT (cf. 9.4.2.1). Therefore, they have been increasingly identified in fatty foods since their discovery. This and the fact that PCBs can produce highly toxic dioxins (cf. 9.10) in the combustion process led to the banning of the production and application of PCBs in 1989. In Germany, the contamination with PCB, e. g., in milk fat (mg/kg) has subsequently fallen on average: 0.012 (1986), 0.007 (1992), 0.003 (2001).

9.7 Harmful Substances from Thermal Processes

9.7.1 Polycyclic Aromatic Hydrocarbons (PAHs)

Burning of organic materials, such as wood (wood smoke and its semi-dry distillation product, the wood smoke vapor phase), coal or fuel oil, results in pyrolytic reactions which yield a great number of polycyclic aromatic hydrocarbons (abouot 250 have been identified) with more than three linearly or angularly fused benzene rings, that are carcinogenic to varying extents. The quantity and diversity of compounds generated is affected by the conditions of the burning process. Benzo[a]pyrene (Bap) (Formula 9.4) usually serves as an indicator compound.



(9.4)

Contamination of food with polycyclic compounds can be caused by fall-out from the atmosphere (as often occurs with fruit and leafy vegetables in industrial districts), by direct drying of cereals with combustion gases, by smoking or roasting of food (barbecuing or charcoal broiling; smoking of sausage, ham or fish; roasting of coffee). PAHs accumulate in high-fat tissues. The content in meat and processed meat products should not exceed 1 µg/kg end-product measured as Bap. A reduction of Bap contamination to this limiting value has been achieved by the use of modern smoking techniques. A maximum of 5 µg/kg Bap is tolerated in smoked fish. Values less than 1.6 µg/kg were found in 95% of the samples tested in food monitoring in 2005.

9.7.2 Furan

Furan is possibly a carcinogenic substance. It occurs in heated food, especially in roasted coffee. Isotopic dilution analyses with [$^2H_4$]-furan as the internal standard yielded 2.5–4.3 mg/kg furan in differently produced coffee powders. Baby food, e.g., carrot mash and potato/spinach mash contained 74 and 75 µg/kg respectively. Furan is formed from amino acids which yield acetaldehyde and glycolaldehyde on thermal degradation (Fig. 9.4). Aldol condensation, cyclization and elimination of water are the reaction steps. Other precursors of furan are carbohydrates, polyunsaturated fatty acids and carotinoids (Fig. 9.4). Furan can also be formed from the thermolysis of ascorbic acid.

9.7.3 Acrylamide

Polyacrylamide, produced from monomeric acrylamide (2-propenamide), has been used for decades in various industrial processes, e. g., as a flocculant in the treatment of drinking water. Especially for reasons of occupational health and safety, numerous toxicological studies on acrylamide have already been conducted. These studies have shown above all that on high exposure, acrylamide (i) binds to hemoglobin in the blood, (ii) is metabolized to reactive epoxide glycidamide and (iii) is carcinogenic on chronic exposure in animal tests. For this reason, acrylamide was put about 20 years ago

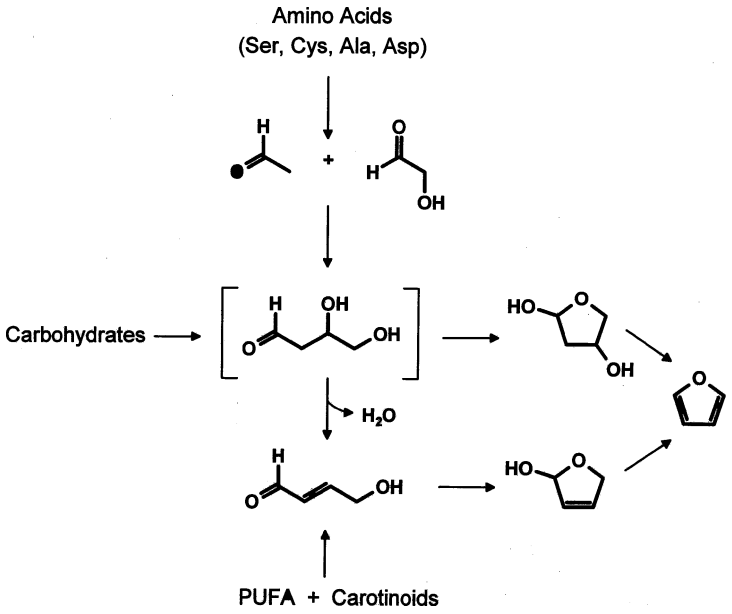


Fig. 9.4. Formation of furan on heating food (according to *Yaylayan*, 2006)

into Category III A2 of carcinogenic working substances. According to EU guidelines for drinking water, the concentration of acrylamide in water should not exceed 0.1 µg/l.

The occurrence of relatively high concentrations of acrylamide in tobacco smoke has been known for a long time, but in 2002 this compound was described for the first time also as a constituent in various thermally treated foods. In particular, processed potato products such as chips, but also fine breads and cakes contain relatively high concentrations (Table 9.11). Today, mainly stable isotope assays in combination with GC–MS or LC–MS with the use of deuterium- or carbon-13-labelled acrylamide are used for the quantitative determination. The large range of variations in the concentrations measured in food indicates that the raw material and the process conditions exert a significant influence on the formation of acrylamide. Thus, it could be shown, e. g., that the formation of acrylamide in potato products clearly fluctuates depending on the variety of potato (Fig. 9.5) and the concentrations of acryl-

Table 9.11. Maximum concentrations and variation ranges of acrylamide in selected foods

Food	Concentration (µg/kg)	
Gingerbread	7800	(80–7800)
Potato chips	3700	(100–3700)
Crispbread	2800	(25–2800)
Roasted nuts	2000	(10–2000)
Ground coffee	500	
Roasted meat	50	
Bread	40	

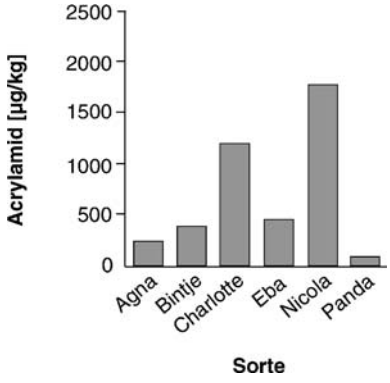


Fig. 9.5. Formation of acrylamide during the frying of potato strips from different varieties of potatoes (according to *Amrein* et al., 2003)

amide can also be distinctly reduced by lowering the heating temperature, e. g., in deep frying. As presented in 1.2.4.4.1, acrylamide is preferentially formed by the reaction of the amino acid asparagine with reductive carbohydrates (or their degradation products). In fact, studies with isotopically labelled asparagine have shown that the carbon skeleton of the amino acid is retained in acrylamide. Nevertheless, the formation of acrylamide, e. g., in the case of potatoes, correlates after heating considerably better with the concentration of fructose and glucose in fresh potatoes than with the concentration of free asparagine although potatoes have a very high concentration of free asparagine at 2–4 g/kg dry weight. In the case of gingerbread, in addition to the concentration of free asparagine, the NH_4HCO_3 used as baking powder was identified as a promoter in the formation of acrylamide.

Apart from the enzymatic hydrolysis of asparagine with asparaginase, the ways in which the content of acrylamide in food can be reduced include the use of various additives, lowering the pH value and reducing the heating temperature. According to more recent calculations, the daily intake of acrylamide from foodstuffs in Germany is assumed to be about 0.57 µg/kg body weight.

9.8 Nitrate, Nitrite, Nitrosamines

9.8.1 Nitrate, Nitrite

The plants which belong to Group A in Table 9.12 can store very much more nitrate than those in Groups B and C, their nitrate content depending among other things on the N supplied on fertilization. Apart from the properties of the soil, even light plays a role because some plants store more nitrate when there is a lack of light. The foods of animal origin listed in Table 9.13 and drinking water (cf. 23.1.3) are a further source of nitrate. It was calculated on the basis of a national consumption study (cf. 9.3.2) that the intake of nitrate is highest in 4–6 year old children (Table 9.14), followed by women and men who prefer fruit and vegetables in their diet rather than meat and fish. The ADI value for nitrate is utilized to 23–40% by the population.

Table 9.12. Nitrate concentrations in vegetables

*A. High concentration (*1000–4000 mg/kg *fresh weight*)
Chinese cabbage, endivie, corn salad, lettuce, fennel, kohlrabi, beetroot, radish, rocket, spinach
*B. Moderate concentration (*500–1000 mg/kg *fresh weight)*
Aubergine, white cabbage, cauliflower, kale, red cabbage and savoy cabbage, leek, carrots, celery, zucchini
C. Low concentration (<500 mg/kg *fresh weight)*
Peas, cereal, green beans, cucumber, potatoes, garlic, fruit, bell peppers, Brussels sprouts, tomatoes, onions

Nitrite mainly comes from cured meat and meat products (Table 9.12). The daily supply amounts to about 0.25 mg $NO_2^{\ominus}$.

It is remarkable that the amount of nitrate formed every day in the human organism, about 1 mg/kg body weight, is just as much as the intake in the diet. The precursor is arginine which is cleaved to give NO and citrullin (cf. 3.7.2.1.8). NO is oxidized to N_2O_3, which reacts with water to give nitrite. Hemoglobin oxidizes nitrite to nitrate, giving rise to methemoglobin which cannot transport oxygen. Therefore, nitrite is toxic, especially for infants (cyanosis) because their methemoglobin reductase still has low activity. This enzyme reduces methemoglobin to hemoglobin.

The toxicity of nitrate starts from the bacterial reduction to nitrite. In the human organism, about 25% of the nitrate absorbed from the food is eliminated with the saliva and up to 7% is reduced to nitrite in the mouth cavity within 24 hours by the action of bacterial nitrate reductases and transported to the stomach. About 90% of the total amount of nitrite which reaches the digestive tract comes from nitrate reduction.

The bacterial formation of nitrite led to the assumption that toxic nitrosamines can arise endogenously by the nitrosation of amines (cf. 9.8.2). This danger has been overestimated. Endogenous nitrosation was described as "practically insignificant" in the nutrition report as early as 1996.

9.8.2 Nitrosamines, Nitrosamides

Nitrosamines and nitrosamides are powerful carcinogens. They are obtained from secondary

Table 9.13. Nitrate and nitrite in milk, cheese and meat products (mg/kg fresh substance)

Food	Nitrate			Nitrite		
	n[a]	Mean	Variation	n[a]	Mean	Variation
Milk	16	1.4	1.0–4.1			
Cheese				39	0.3	0.2–1.3
Meat	110	7.6	1.0–49.5			
Uncooked smoked pork ribs	73	68.6	5.0–425.5	47	27.9	0.2–94.1
Uncooked smoked black forest ham	23	351.0	21.6–1384.3	20	12.3	1.2–80.2
Uncooked smoked ham				23	10.7	0.9–44.2
Uncooked sausages, firm	20	208.4	7.0–1042.0			
Cooked smoked shoulder ham				44	15.7	0.8–91.0
Salami				76	5.1	0.3–48.7
Fresh soft sausage				35	6.9	0.2–45.6
Fried sausage				108	3.5	0.2–41.5
Finely minced pork sausage				32	7.8	0.2–18.6
Calf-liver sausage, finely grained				19	5.4	1.9–12.3
Salted herring filet	154	27.4	1.0–405.0			
Herring titbit	103	74.7	19.0–276.0			

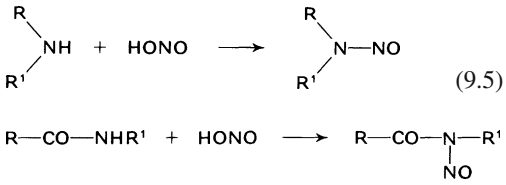
[a] Number of samples.

Table 9.14. Intake of nitrate and utilization of the reference value (food monitoring 1995–2002)

Group of persons	Intake		Utilization
	(mg/d)	(mg/kg kg/d)	%-ADI[a]
Children, 4–6 years	30.6	1.465	40.1
Children, 7–10 years	37.7	1.220	33.4
Men	64.6	0.830	22.7
Men, fish eaters	69.0	0.862	23.6
Men, meat eaters	73.3	0.921	25.2
Men, fruit and vegetable eaters	90.8	1.155	31.6
Women	61.0	0.950	26.0
Women, fish eaters	67.8	1.034	28.3
Women, meat eaters	70.0	1.064	29.2
Women, fruit and vegetable eaters	86.2	1.328	36.4

[a] The ADI value for nitrate is 3.65 mg/kg kg/d.

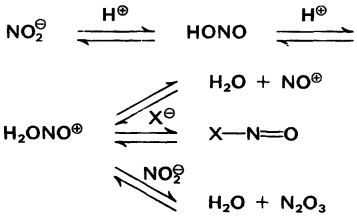
amines, N-substituted amides and nitrous acid:



(9.5)

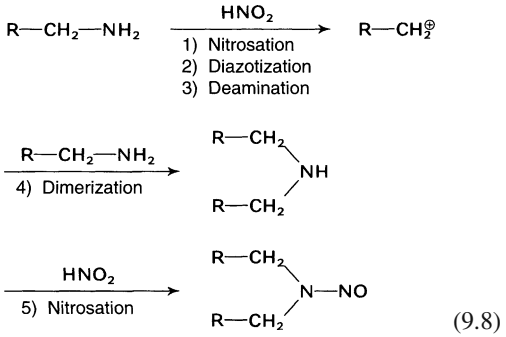
(9.6)

The nitrosonium ion, NO^+, or a nitrosyl halogenide, XNO, is the reactive intermediate:



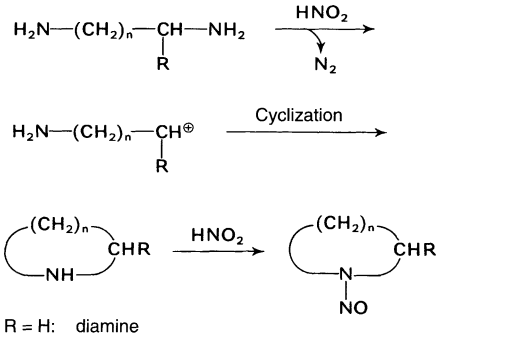
(9.7)

Nitrosamine formation is also possible from primary amines:



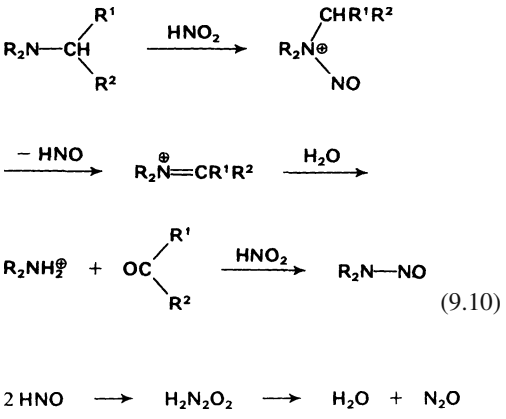
(9.8)

from diamines:



(9.9)

and from tertiary amines:



(9.10)

(9.11)

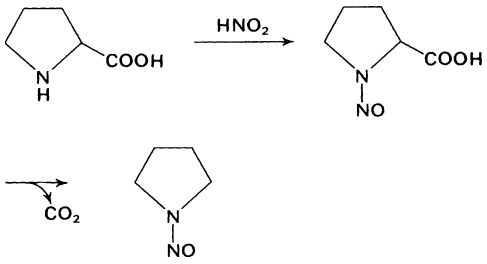
Table 9.15. Nitrosamines in food

Food product	Compound[a]	Content µg/kg
Frankfurter (hot dog)	NDMA	0–84
Fish (raw)	NDMA	0–4
Fish, smoked and pickled with nitrites or nitrates	NDMA	4–26
Fish, fried	NDMA	1–9
Cheese (Danish, Blue, Gouda, Tilsiter, goatmilk cheese)	NDMA	1–4
Salami	NDMA	10–80
Bacon (hog's hind leg) smoked meat	NDMA	1–60
Pepper-coated ham, raw and roasted	NPIP	4–67
	NPYR	1–78

[a] NDMA: N-Nitrosodimethylamine, NPIP: N-nitrosopiperidine, NPYR: N-nitrosopyrrolidine.

Nitrosamines are detected in variable amounts in many foods (Table 9.15). The most common compound is dimethylnitrosamine, which is also a most powerful carcinogen. Some activity has been ascribed to nitrosopiperidine and nitrosopyrrolidine. In meat products cured and treated with pickling salt, 30% of the samples contained nitrosodimethylamine (NDMA; 0.5–15 µg/kg) and 13% nitrosopyrrolidine (NPYR; >0.5 µg/kg). About 25% of the cheese samples analyzed were contaminated (0.5–4.9 µg/kg).

Nitrosopyrrolidine is formed from the amino acid proline by nitrosation followed by decarboxylation at elevated temperatures, such as in roasting or frying:



(9.12)

Table 9.16. Amines in food (mg/kg)

		Cabbage (kale)							Herring			Cheese		
Compound	Spinach	red	green	Carrots	Red beet	Celery	Lettuce	Rhubarb	salted	smoked	in oil	Tilsiter	Camembert	Limburger
Ammonia	18.280	11.060	15.260	3.970	8.800	19.600	10.260	6.340	2.928	270	–	164.400	–	–
Methylamine	12	22.7	16.6	3.8	30	64	37.5	–	3.4	–	7	–	12	3
Ethylamine	8.4	1.3	–	1	–	–	3.3	0.1	0.4	0.4	–	–	4	1
Dimethylamine	–	2.8	5.5	–	–	51	7.2	–	7.8	6.3	45	–	–	–
Methylethylamine	–	0.9	–	7	–	–	7.5	–	–	–	1	–	–	–
n-Propylamine	–	–	–	–	–	–	–	–	–	–	–	8.7	2	2
Diethylamine	15	–	–	–	–	–	–	–	1.9	5.2	–	–	–	–
n-Butylamine	–	–	7	–	–	–	–	–	–	–	–	3.7	–	–
i-Butylamine	–	–	–	–	–	–	–	–	–	0.3	–	–	0.2	0.2
Pyrroline	–	–	–	–	–	–	–	–						
n-Pentylamine	0.3	0.6	0.4	–	–	0.8	3	–	–	–	17	1.2	–	–
i-Pentylamine	3.8	–	0.5	–	–	–	–	3.9	–	–	–	–	0.2	tr[a]
Pyrrolidine	2.5	–	–	–	–	0.4	–	–	–	–	–	19.9	1	0.1
Di-n-propylamine									–	–	–	8.4	–	–
Piperidine									0.7	0.2	–	–	–	tr
Aniline	–	1.0	0.7	30.9	0.6	0.7	0.6	5						
N-Methylaniline	3.4	0.3	–	0.8	–	0.5	–	–	–	–	–	37.9	–	–
N-Methylbenzylamine	–	–	–	16.5	–	–	10	–	–	–	2	–	–	–
Toluidine	–	–	1.1	7.2	–	1.1	–	–						
Benzylamine	6.1	3.3	3.8	2.8	0.1	3.4	11.5	2.9						
Phenylethylamine	1.1	8.6	3	2	0.5	–		3.2						
N-Methylphenylethylamine	2.4	3.7	2	2	0.4	0.5	0.4	2.6	–	–	0.1	2.6	–	–

[a] Traces.

The nitrosopyrrolidine (1.5 µg/kg) in meat products increases almost ten fold (to 15.4 µg/kg) during roasting and frying. An estimate of the average daily intake of nitrosamines ranges from 0.1 µg nitrosodimethylamine and 0.1 µg nitrosopyrrolidine to a total of 1 µg.

The concentrations in food of ammonia and amines which can possibly undergo nitrosation are presented in Table 9.16.

Inhibition of a nitrosation reaction is possible, e. g., with ascorbic acid, which is oxidized by nitrite to its dehydro form, while nitrite is reduced to NO. Similarly, tocopherols and some other food constituents inhibit substitution reactions. Representative suitable measures to decrease exo- and endogenic nitrosamine hazards are:

- Decreasing nitrite and nitrate incorporation into processed meat. However, to completely relinquish the use of nitrite is a great health hazard due to the danger from bacterial intoxication (especially by botulism).
- Addition of inhibitors (ascorbic acid, tocopherols).
- Decreasing the nitrate content of vegetables.

9.9 Cleansing Agents and Disinfectants

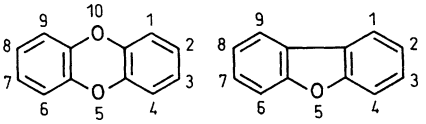
Residues introduced by large-scale animal husbandry and use of milking machines are gaining importance. The residues in meat and processed meat products originate from the surfaces of processing equipment, while residues in milk arise from measures involved in disinfection of the udder. Iodine-containing disinfectants, including udder dipping or soaking agents, may be an additional source of contamination of milk with iodine.

Also in the case of fruit and vegetables, measures have to be taken to kill pathogenic microbes. Although chlorine is normally used, it does not kill all the bacteria in the permitted concentrations. In addition, chlorine can convert pesticide residues to substances of unknown biological activity. *Ozone* is recommended as an alternative. In disinfection, it is 1.5 times as active as chlorine, kills microorganisms which are not attacked by chlorine and destroys pesticide residues. It decomposes to molecular oxygen with a half

life (aqueous ozone solution) of 20 minutes at room temperature. To disinfect process water, 0.5–5 mg/kg of ozone are used for <5 minutes. Apart from disinfection, ozone also delays the ripening of fruit (cf. 18.1.4.1).

9.10 Polychlorinated Dibenzodioxins (PCDD) and Dibenzofurans (PCDF)

Polychlorinated dibenzo-p-dioxins (PCDD) and polychlorinated dibenzofurans (PCDF), informally called "dioxins", occur as companion compounds or impurities in a large number of bromine- and chlorine-containing chemicals.



(9.13)

Furthermore, they are formed in many thermal processes ($600\,^{\circ}C > T \geq 200\,^{\circ}C$) in the presence of chlorine or other halogens in inorganic or organic form. Consequently, they are widely distributed in the environment. The number of isomers (congeners) is large, For rodents, 2,3,7,8-tetrachlorodibenzodioxin (2,3,7,8-TCDD, "Seveso dioxin") has proved to be expecially toxic ($LD_{50} = 0.6\,\mu g/kg$, guinea-pig) and carcinogenic. With the exception of PnCDD, the toxicity of other congeners is lower and is generally expressed as toxicity equivalent factors (TEFs), based on 2,3,7,8-TCDD (TEF = 1) (Table 9.17). With the help of these values, 2,3,7,8-TCDD equivalents (TCDD equivalents, TEQ) can be calculated, which are a measure of the total exposure to corresponding compounds (cf. Table 9.17 and 9.18).

The daily intake of dioxin in industrial countries is estimated at 1–3 pg TEQ/kg body weight. The half life and the absorption rate are assumed to be 7.5 years and 50% respectively. In 1997, the WHO set a value of 1–4 pg TEQ per kg body weight and day as a tolerable, lifelong intake (tolerable daily intake, TDI). Table 9.18 shows the estimated dioxin intake with food. Due to the concentration of dioxins in the fat phase, mother's milk in the industrial countries has on average 10–35 pg TEQ per g of fat and in the developing countries, 10 pg TEQ per g of fat.

Table 9.17. Risk assessment of dibenzo-p-dioxins and dibenzofurans

Congener	TEF[a]
Dibenzo-p-dioxins	
2,3,7,8-TCDD	1
1,2,3,7,8-PnCDD	1
1,2,3,4,7,8-HxCDD	0.1
1,2,3,6,7,8-HxCDD	0.1
1,2,3,7,8,9-HxCDD	0.1
1,2,3,4,6,7,8-HpCDD	0.01
OCDD	0.0001
Dibenzofurans	
2,3,7,8-TCDF	0.1
1,2,3,7,8-PnCDF	0.05
2,3,4,7,8-PnCDF	0.5
1,2,3,4,7,8-HxCDF	0.1
1,2,3,6,7,8-HxCDF	0.1
1,2,3,7,8,9-HxCDF	0.1
2,3,4,6,7,8-HxCDF	0.1
1,2,3,4,6,7,8-HpCDF	0.01
1,2,3,4,7,8,9-HpCDF	0.01
OCDF	0.0001

[a] Toxicity equivalent factors (2,3,7,8-TCDD = 1).

Table 9.18. Average daily intake of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) and related compounds with the food (pg/day)[a]

	2,3,7,8-TCDD	ΣTEQ[b]
Meat products (including poultry)	7	23.5
Milk	6.2	28.5
Eggs	0.8	4.2
Fish	8.6	33.3
Vegetable oil	<0.2[c]	<0.6
Vegetables	<2.4[c]	<2.4[c]
Fruits	<1.4[c]	<2.6[c]
Sum:	24.6	93.5[d]

[a] Based on an "average food basket".
[b] Sum of the compounds taken in, expressed as toxicity equivalents TEQ (cf. text).
[c] These numbers are included in the sum with 50%.
[d] At present, the TDI value (cf. text) is 1–4 pg/kg body weight and day. In outdoor air that is not directly contaminated, it can be assumed that the intake through breathing is 0.03 pg TEQ/kg body weight and day.

9.11 References

Ames, B.N., Gold, L.S.: Paracelsus to parascience: the environmental cancer distraction. Mutation Research *447*, 3 (2000)

Amrein, T., Bachman, S., Noti, A., Biedermann, M., Barbarosa M.M., Biedermann-Brem, S., Grob, K., Keiser, A., Realini P., Scher, E., Amado, R.: Potential of acrylamide formation, sugars, and free asparagine in potatoes: a comparison of cultivars and farming systems. J. Agric. Food Chem. *51*, 5556 (2004)

Anastassiades, M., Lehotay, S.J., Stajnbaher, D., Schenk, F.J.: Fast and easy multiresidue method employing acetonitrile extraction/partitioning and "dispersive solid-phase extraction" for the determination of pesticide residues in produce. JAOAC internat *86*, 412 (2003)

Atreya, N.: Does the mere presence of a pesticide residue in food indicate a risk? J. Envir. Monit. *2*, 53N (2000)

Ballschmiter, K.: Chemie und Vorkommen der halogenierten Dioxine und Furane. Nachr. Chem. Tech. Lab. *39*, 988 (1991)

Beckmann, M., Haack, K.-J.: Insektizide für die Landwirtschaft. Chemie in unserer Zeit *37*, 88 (2003)

Buchanan, R.L., Doyle, M.P.: Food borne disease significance of Escherichia coli 0157:H7 and other enterohemorrhagic E. coli. Food Technol. *51* (no. 10), 69 (1997)

Bundesamt für Verbraucherschutz und Lebensmittelsicherheit: Ergebnisse des bundesweiten Lebensmittel-Monitorings der Jahre 1995–2002. www.bvl.bund.de/dl/monitoring/monitoring-1995-2002.pdf

Bundesforschungsanstalt für Ernährung: Radioaktivität in Lebensmitteln – Tschernobyl und die Folgen. Bericht BFE-R-86-04, Karlsruhe, Dezember 1986

Cikryt, P.: Die Gefährdung der Menschen durch Dioxine und verwandte Verbindungen. Nachr. Chem. Tech. Lab. *39*, 648 (1991)

Diehl, J.F.: Chemie in Lebensmitteln – Rückstände, Verunreinigungen, Inhalts- und Zusatzstoffe. Wiley-VCH-Verlag, Weinheim, 2000

Dixon, S.N.: Veterinary drug residues. In: Food chemical safety. Vol. 1: Contaminants (Ed. D.H. Watson). Woodhead Publishing, Cambridge, England, 2001, p. 109

Eisenbrand, G.: N-Nitrosoverbindungen in Nahrung und Umwelt. Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart, 1981

Hathway, D.E.: Molecular aspects of toxicology. The Royal Society of Chemistry, Burlington House, London, 1984

Henningsen, M.: Moderne Fungizide. Chemie in unserer Zeit *37*, 98 (2003)

Macholz, R., Lewerenz, H.: Lebensmitteltoxikologie. Springer-Verlag, Berlin, 1989

National Research Council (U.S.A.): Regulating Pesticides in Food. National Academy Press, Washington, D.C., 1987

Petz, M.: Tandem-MS; Biosensoren und weitere analytische Trends sowie jüngste Erkenntnisse bei Tierarzneimittelrückständen. Lebensmittelchemie *55*, 1 (2001)

Petz, M.: Toxikologische Aspekte der Ernährung. In: Ernährungsbericht 2004. Deutsche Gesellschaft für Ernährung (ed.), p. 119

Rychlik, M., Schieberle, P.: Quantification of the mycotoxin Patulin by a stable isotope dilution assay. J. Agric. Food Chem. *47*, 3749 (1999)

Schrenk, D., Fürst, P.: WHO setzt Werte für die tolerierbare tägliche Aufnahme an Dioxinen neu fest. Nachr. Chem. Techn. Lab. *47*, 313 (1999)

Schwack, W., Anastassiades, M., Scherbaum, E.: Rückstandsanalytik von Pflanzenschutzmitteln. Chemie in unser Zeit *37*, 324 (2003)

Seitz, T., Hoffmann, M.G., Krähmer, H.: Herbizide für die Landwirtschaft. Chemie in unserer Zeit *37*, 112 (2003)

U.S. Food and Drug Administration: Pesticide Program. Residue Monitoring 2002. www.cfsan.fda.gov/dms/pres02rep.html

Von Hoof, N., de Wasch, K., Hoppe, H., Poelmans, S., de Brabander, H.F.: In: Rapid and on-line instrumentation for food quality assurance (Ed.: I.E. Tothill). Woodhead Publishing, Cambridge, 2002, p. 91

Wettach, J.W., Rung, B., Schwack, W.: Detection of photochemically induced cuticle-bound residues of parathion by immunoassay. Food Agric. Immunol. *14*, 5 (2002)

Xu, L.: Use of ozone to improve the safety of fresh fruits and vegetables. Food Technol. *53* (10), 58 (1999)